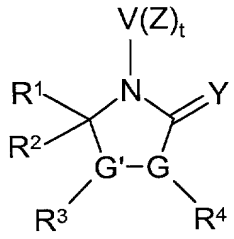
We claim

1. A pharmaceutical composition comprising a compound according to formula I



wherein,

Y is oxygen or sulfur;

G and G', together with the bond linking them, are HC – CH or C = C;

V is aryl, heterocycle or cycloalkyl;

Z is halogen, alkyl, alkenyl, alkynyl, hydroxyl, amino, alkoxy, aryloxy, nitro or cyano;

R^1 is hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl or heterocycle;

R^2 is hydrogen or hydroxy;

R^3 is $-C(O)R^{3a}$, $-S(O)_2R^{3a}$, $-S(O)R^{3a}$ or SR^{3a} wherein R^{3a} has the same meaning as R^1;

R^4 is hydroxy or amino;

t is 0, 1, 2, 3, 4 or 5;

or a pharmaceutically acceptable salt or metabolically cleavable derivative thereof, together with a phamaceutically acceptable diluent or carrier.

2. A composition according to claim 1 wherein in the formula I

Y is oxygen,

G and G', together with the bond linking them, are C = C,

and the meaning of V is selected from,

a) aryl, especially phenyl, benzyl, naphthyl, naphthylmethyl, indenyl, dihydro indenyl; heterocycle especially pyridyl;

b) phenyl, benzyl, naphthyl, naphthylmethyl, indenyl, dihydro indenyl or pyridyl;

c) phenyl, benzyl or dihydroindenyl;

d) phenyl or dihydroindenyl;

e) phenyl or benzyl; and

f) phenyl.

3. A composition according to claim 1 wherein in the formula I

Y is oxygen,

G and G', together with the bond linking them, are C = C,

and the meaning of Z is selected from,

a) halogen, alkyl, alkoxy, OH, NO_2 or NH_2;

b) halogen, alkyl, alkoxy, NO_2 or NH_2;

c) fluoro, chloro, bromo, iodo, C_{1-4}-alkyl, C_{1-4} alkoxy, trifluoromethyl, NO_2 or NH_2;

d) fluoro, chloro, bromo, iodo, C_{1-4}-alkyl, methoxy, trifluoromethyl, NO_2 or NH_2;

e) fluoro, chloro, bromo, C_{1-4}-alkyl, C_{1-4} alkoxy, trifluoromethyl, NO_2 or NH_2;

f) fluoro, chloro, bromo, C_{1-4}-alkyl, methoxy, trifluoromethyl, NO_2 or NH_2;

g) fluoro, chloro, bromo, iodo, C_{1-4} alkyl;

h) fluoro, chloro, bromo, iodo, methyl or ethyl;

i) fluoro, chloro, bromo, C_{1-4} alkyl; and

j) fluoro, chloro, bromo, methyl or ethyl.

4. A composition according to claim 1 wherein in the formula I

Y is oxygen,

G and G', together with the bond linking them, are C = C, and t is selected from,

a) 1, 2 or 3; and

b) 1 or 2.

5. A composition according to claim 1 wherein in the formula I

Y is oxygen,

G and G', together with the bond linking them, are C = C,

and the meaning of R^1 is selected from,

a) alkyl, cycloalkyl, cycloalkenyl, optionally substituted phenyl or heterocycle;

b) C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{6-8} cycloalkenyl, optionally substituted phenyl or heterocycle;

c) C_{1-8} alkyl, C_{3-8} cycloalkyl, C_{6-8} cycloalkenyl, furyl, thienyl or phenyl, optionally substituted by one or more alkyl or halogen,;

d) methyl, ethyl, propyl, i-propyl, 3,3,3-trifluoropropyl, i-butyl, t-butyl, pentyl, 1-ethylpropyl, neo-pentyl, 1,2-dimethylbutyl or 1-propylbutyl, cyclopropyl, cyclopentyl, cyclohexyl, cyclohexylmethyl, cycloheptyl, cyclooctyl or adamantyl, 2-cyclohexenyl or bicyclo[2.2.1]hept-5-enyl, furyl, thienyl or phenyl, optionally substituted by one or more alkyl or halogen; and

e) 1-ethylpropyl, cyclohexyl, phenyl, optionally substituted by one or methyl, fluoro, chloro bromo or cyano;

6. A composition according to claim 1 wherein in the formula I
Y is oxygen,
G and G', together with the bond linking them, are C = C,
and R^2 is hydrogen.

7. A composition according to claim 1 wherein in the formula I
Y is oxygen,
G and G', together with the bond linking them, are C = C,
and R^3 is $-C(O)R^{3a}$ wherein the meaning of R^{3a} is selected from,

a) alkyl, optionally substituted aryl or heterocycle;

b) C_{1-5}-alkyl, optionally substituted phenyl, benzyl, phenethyl, phenylamino or thienyl; and

c) methyl.

8. A composition according to claim 1 wherein in the formula I
Y is oxygen,
G and G', together with the bond linking them, are C = C,
and R^4 is hydroxy.

9. A composition according to claim 1 wherein the compound of formula I is selected from those numbered 10, 13, 17, 18, 24, 25, 51, 53, 54, 56, 63, 65, 69, 70, 72, 79, 118, 119, 120, 121 and 125 in Table 1.

10. A composition according to claim 9 wherein the compound of formula I is selected from those numbered 10, 17, 18, 24, 51, 53, 54, 69, 72, 118, 119, 120 and 125 in Table 1.

11. A composition according to claim 1 wherein the compound of formula I is in the form of its (-)-enantiomer.

12. A compound of formula I as illustrated in claim 1 wherein, X is CH; and the remaining substituents are as defined in claim 1.

13. A compound of formula I as illustrated in claim 1 wherein, Y is sulphur; and the remaining substituents are as defined in claim 1.

14. A compound of formula I as illustrated in claim 1 wherein, R^1 is hydrogen, halogen, alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, aryl or heterocycle and R^2 is hydroxy and the remaining substituents are as defined in claim 1.

15. A compound of formula I as illustrated in claim 1 wherein, R^1 is as defined above except for hydrogen, C_1-$_7$-alkyl, phenyl, C_3-$_5$-cycloalkyl, or methylene (C_3-$_5$-cycloalkyl) wherein each alkyl or phenyl group may be substituted with one or two methyl, methoxy, ethyl or trifluoromethyl, or up to three halogens and R^2 is hydrogen and the remaining substituents are as defined in claim 1.

16. A compound of formula I as illustrated in claim 1 wherein, one of R^1 and R^2 is other than hydrogen and the remaining substituents are as defined in claim 1.

17. A compound of formula I as illustrated in claim 1 wherein R^3 is as defined in claim 1 except for -C(O)R^{3b} wherein R^{3b} is hydrogen, C_1-$_7$-alkyl, C_2-$_3$-alkenyl, phenyl, C_3-$_5$-cycloalkyl, or methylene (C_3-$_5$-cycloalkyl) wherein each alkyl, phenyl or alkenyl group may be substituted with one nitro, methoxy or ethoxy, with one or two methyl, ethyl or

trifluoromethyl, or with up to three halogens and the remaining substituents are as defined in claim 1.

18. A compound of fomula I as defined in claim 1 wherein when

X is nitrogen;

Y is oxygen; and

G and G', together with the bond linking them, are C = C; then

R^1 is other than hydrogen, C_{1-7}-alkyl, phenyl, C_{3-5}-cycloalkyl, or methylene (C_{3-5}-cycloalkyl) wherein each alkyl or phenyl group may be substituted with one or two methyl, methoxy, ethyl or triflouromethyl, or up to three halogens when R^2 is hydrogen; or

R^3 is other than -C(O)R^{3b} wherein R^{3b} is hydrogen, C_{1-7}-alkyl, C_{2-3}-alkenyl, phenyl, C_{3-5}-cycloalkyl, or methylene (C_{3-5}-cycloalkyl) wherein each alkyl, phenyl or alkenyl group may be substituted with one nitro, methoxy or ethoxy, with one or two methyl, ethyl or trifluoromethyl, or with up to three halogens.

19. A compound of formula I as illustrated in claim 1 in fully or partially resolved isomeric form.

20. A compound of formula I as illustrated in claim 1 which is selected from the compounds of Table 1 except for those numbered 1, 2, 3, 4, 5, 9 and 122.

21. A method of treating or preventing conditions mediated by CCR2, MCP-1 or the interaction thereof, the method comprising administering to a patient an amount of a CCR2 antagonist sufficient to prevent, reduce or eliminate the condition.

22. A method according to claim 21 wherein the CCR2 antagonist is a compound of formula I as defined in claim 1 or a pharmaceutically active derivative or salt thereof.

23. A method of treating or preventing conditions mediated by CCR2, MCP-1 or the interaction thereof, the method comprising administering to a patient an amount of a compound of formula I as defined in claim 1, or a pharmaceutically active derivative or salt thereof, sufficient to prevent, reduce or eliminate the condition.

24. A method according to claim 21 wherein the condition is selected from asthma, seasonal and perennial allergic rhinitis, sinusitus, conjunctivitis, food allergy, scombroid poisoning, psoriasis, urticaria, pruritus, eczema, inflammatory bowel disease, chronic obstructive pulmonary disease, thrombotic disease, otitis media, neuroinflammatory diseases such as multiple sclerosis, atherosclerosis, other inflammatory diseases such as rheumatoid arthritis and nephritis, liver cirrhosis, cardiac disease, pulmonary fibrosis, valvular restenosis, Alzheimer's disease, sepsis, systemic sclerosis and ulcerative colitis.

25. A method according to claim 23 wherein the condition is selected from asthma, seasonal and perennial allergic rhinitis, sinusitus, conjunctivitis, food allergy, scombroid poisoning, psoriasis, urticaria, pruritus, eczema, inflammatory bowel disease, chronic obstructive pulmonary disease, thrombotic disease, otitis media, neuroinflammatory diseases such as multiple sclerosis, atherosclerosis, other inflammatory diseases such as rheumatoid arthritis and nephritis, liver cirrhosis, cardiac disease, pulmonary fibrosis, valvular restenosis, Alzheimer's disease, sepsis, systemic sclerosis and ulcerative colitis.

26. A method according to claim 24 wherein the condition is asthma.

27. A method according to claim 25 wherein the condition is asthma.